

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference GMW/G2161WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/JP 03/10054	International filing date (<i>day/month/year</i>) 07.08.2003	Priority date (<i>day/month/year</i>) 08.08.2002
International Patent Classification (IPC) or both national classification and IPC C07D215/00, C07D215/00		
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

I ☒ Basis of the opinion

II ☐ Priority

III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

IV ☐ Lack of unity of invention

V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

VI ☐ Certain documents cited

VII ☐ Certain defects in the international application

VIII ☐ Certain observations on the international application

Date of submission of the demand 12.09.2003	Date of completion of this report 02.06.2004
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>	Authorized Officer Usuelli, A Telephone No. +49 89 2399-7366



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/JP 03/10054**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-240 as originally filed

Claims, Numbers

1-28 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/JP 03/10054

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1(part),3(part)-8(part), 10(part)-28(part)

because:

- ☒ the said international application, or the said claims Nos. 17-21 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
☒ no international search report has been established for the said claims Nos. 1(part),3(part)-8(part),10(part)-28(part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.
☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-28
	No: Claims	
Inventive step (IS)	Yes: Claims	1-28
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-16, 22-28
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1- Claims 17-21 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims, cf. Article 34(4)(a)(i) PCT.

2- The preliminary examination report will be limited to the parts of the application which have been searched (Rule 66.1(e) PCT, see also Box 1.2 of the search report).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1- Reference is made to the following documents:

- D1: WO 98/19998 A (CIBA GEIGY AG ; VILLHAUER EDWIN BERNARD (US))
14 May 1998 (1998-05-14)
- D2: AUGUSTYNS K ET AL: "THE UNIQUE PROPERTIES OF DIPEPTIDYL-
PEPTIDASE IV (DPP IV/CD26) AND THE THERAPEUTIC POTENTIAL OF
DPP IV INHIBITORS" CURRENT MEDICINAL CHEMISTRY, BENTHAM
SCIENCE PUBLISHERS BV, BE, vol. 6, no. 4, 1999, pages 311-327,
XP000870290 ISSN: 0929-8673

2- Novelty

Present compounds of formula (I) differ from the compounds disclosed in d1 and d2 at least on account of the quinoline ring. The searched parts of claims 1 to 28 are therefore considered to meet the requirements of Art.33.2 PCT.

3- Inventive step

3.1- The applicant has set himself the task of providing novel DPP-IV inhibitors having potential use in the treatment of diabetes.

Documents d1 and d2 relate to compounds having the same use of present compounds. D1 is regarded as the closest state of the art.

For the purpose of assessing the inventive step during the international phase it is accepted that substantially all the compounds of formula (I) possess the claimed

activity, i.e. they inhibit the dipeptidyl dipeptidase IV.

Thus, the objective technical problem may be seen in the provision of further DPP-IV inhibitors.

3.2- The compounds of d1 are N-substituted-2-cyanopyrrolidine derivatives. Also the DPP IV inhibitors disclosed in Fig. 4 of d2 are N-substituted pyrrolidine derivatives. Neither d1 nor d2 disclose compounds containing a quinoline ring.

Hence, it appears that the skilled person faced with the technical problem defined above would not find in the prior art's documents any hint for preparing the compounds of formula (I).

The requirements of Art.33.3 are therefore met.